

Reversibility and Non-reversibility in Stochastic Chemical Kinetics

V. A. Malyshev, S. A. Pirogov

Abstract

Mathematical problems with mean field and local type interaction related to stochastic chemical kinetics are considered. Our main concern is various definitions of reversibility, their corollaries (Boltzmann type equations, fluctuations, Onsager relations, etc) and emergence of irreversibility.

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1 Introduction

It is known that any closed dynamical system has sufficiently simple behavior - 'it tends to equilibrium'. One of the reasons for such a behavior is 'time reversibility of the dynamics'. In biology we have completely different, more complicated, behavior. Standard approach of biological and chemical theories to explain complicated biological phenomena is to select some suitable non-reversible system of chemical reactions. It is rather clear that in such a way any behavior can be explained, that reduces the value of the theory. At the same time, any non-reversible system of reactions can be formally deduced from (reversible) laws of physics only under some scaling limits.

In this review we discuss mathematical problems related to the reversibility and non-reversibility of chemical reaction systems.

In section 2 we consider connections between various probabilistic characteristics of chemical reaction systems. We give classical and stochastic description of chemical reaction system. Classical chemical kinetics is the core of any theoretical and applied investigations in biology. Stochastic chemical kinetics had always been more theoretical, however also its applied aspect emerges, see [4, 3, 5]. We study how the fact of the invariance of Poisson measure is related to 3 main variants of reversibility for chemical reaction systems: chemical reversibility, reversibility as in Markov processes theory and unitarity. At the end of the section we touch the (yet non developed) case of large number of molecule types.

The main question is how chemical reaction systems behave for large times. In section 3 it is shown that, under the reversibility assumption this behavior is rather simple - the system tends to a fixed point, that is to equilibrium. Dynamics in the vicinity of the fixed point is normally described by two physical theories: linear perturbations which bring us to Onsager relations, and even smaller perturbations - stochastic fluctuations. We present here rigorous versions of these theories. Finally, we present two ways of emergence of non-reversibility in chemical reaction systems - transport and time scaling.

In physics, a well-known procedure to get non-reversibility is the limiting transition to Boltzmann equation. Stochastic and classical chemical kinetics are typical examples of the theories which are called mean field theories in physics. In section 4 we consider various possibilities of how to introduce locality in chemical reaction systems with infinite number of particles. We specify 3 kinds of scaling which give deterministic quasilinear partial differential equations with nonlinear term similar to the right-hand part of the equations (3) of classical chemical kinetics:

1. canonical scaling with $M \rightarrow \infty$ in chemical kinetics, where simultaneously the particles move in the space;
2. the Boltzmann-Grad limit in the particle system with local chemical reactions;
3. standard hydrodynamic scaling for particle systems performing random walk on a lattice.

In Newtonian and quantum mechanics the notion of reversibility is different and natural question is how this is related to previous definitions. We touch this in section 5. Moreover, in all models of chemical kinetics, considered in earlier sections, the reactions are instant events. In fact however, reactions takes some time interval which in both classical and quantum scattering theories is even formally infinite. This means that scattering theory and chemical kinetics lie on different timescales, sufficiently separated from each other. In despite of this, the reaction intensities should be possible to calculate from mathematical scattering theory. At the end of section 5 we introduce the notion of metastable particle, that is a particle with finite life time, not as a singularity (resonance) in the spectrum of a finite particle operator, but how some local formation in the infinite particle system.

2 Stochastic chemical kinetics

2.1 Stochastic and classical description of chemical reactions

Assume there are finite molecule types $A_v, v = 1, \dots, V$. The chemical reaction r is defined by the vectors $d_-(r) = \{d_-(v, r)\}, d_+(r) = \{d_+(v, r)\}$ of stoichiometric coefficients, where the non-negative integers $d_-(v, r)$ are the multiples of the substrate A_v of type v , $d_+(v, r)$ are the multiples of the product of type v . The reactions is written formally as

$$\sum_v d_-(v, r) A_v \rightarrow \sum_v d_+(v, r) A_v$$

Consider the system of chemical reactions, that is the Markov process \mathcal{M} with the states $n = (n_1, \dots, n_V)$ and R transitions (reaction types) $r = 1, 2, \dots, R$

$$n_v \rightarrow n_v + d_+(v, r) - d_-(v, r), v = 1, \dots, V \quad (1)$$

where n_v is the number of molecules of type v .

Here we should do the following comment. Below in section 5, especially in 5.3, we discuss how the given stochastic model of chemical kinetics is related to the basic principles of physics. Note however that there is no rigorous deduction of this model from basic postulates. Here two problems appear. The first one is related in stochastic chemical kinetics the time scale is coarser comparative with

the time of one reaction. This time can be calculated using quantum scattering theory. However, even for the simplest reactions such calculations are sufficiently complicated and, moreover, the separation of these two scales had never been realized in a rigorous way. This would be sufficient to deduce the local models considered below in sections 4, from the first principles. However in sections 2 and 3 we consider mean field models. And the second problem is how the mean field models are related to local models. We do not give answer to this question, which appears always when in physics one uses mean field models. One should say however that the limiting Boltzmann equations in mean field and local case differ only by renormalization of the reaction intensities. An intermediate case could be the Kac model where the molecule can react not with each other, but only with molecules situated on a distance not bigger than ϵL , where L is the diameter of the system.

The reaction r , that is the transition (1), has the rate (speed of the reaction in chemical kinetics)

$$\lambda_r(n) = \lambda_r(n \rightarrow n - d_-(r) + d_+(r)) = M^{-m_-(r)+1} a_r \prod_{v \in I(r)} n_v \dots (n_v - d_-(v, r) + 1), \quad (2)$$

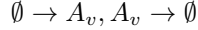
where a_r are the fixed numbers (constants of the speed in chemical kinetics), M is the scaling coefficient, and

$$m_-(r) = \sum_v d_-(v, r), I(r) = \{v : d_-(v, r) > 0\}$$

The power of M in (2) corresponds to the so called canonical scaling, as defined in [17].

Note that equation (2) expresses the law of mass action, well-known in chemical kinetics.

We will also consider distinguished reactions “input” and “output”



with the rates $M a_{v,in}$ and $a_{v,out} n_v$ correspondingly. If there are no such reactions in the system, we will call the system closed, otherwise open.

Note shortly that the history of stochastic chemical kinetics starts with the paper [6], the subsequent story consisted mainly in the study of systems with small R and V , see references in [7, 8].

2.1.1 Convergence to the equations of classical kinetics

Classical kinetics can be obtained from the stochastic one in the limit $M \rightarrow \infty$. Namely, we consider the family of processes $n_v(t) = n_v^{(M)}(t)$, depending on the parameter M . We cite here the well-known result, see references in [17], under more general assumptions, including possible input and output.

Theorem 1 *Assume that initially the limits*

$$c_v(0) = \lim_{M \rightarrow \infty} \frac{n_v(0)}{M}$$

exist for all v . Then for any v and $t > 0$ there exist the following limits in probability

$$c_v(t) = \lim_{M \rightarrow \infty} \frac{n_v(t)}{M}$$

which satisfy the following equations (the standard equations of chemical kinetics)

$$\frac{dc_v(t)}{dt} = \sum_{r: v \in O(r)} d_+(v, r) a_r \prod_{w \in I(r)} c_w^{d_-(w, r)} - \sum_{r: v \in I(r)} d_-(v, r) a_r \prod_{w \in I(r)} c_w^{d_-(w, r)} \quad (3)$$

where

$$O(r) = \{v : d_+(v, r) > 0\}$$

The conservation laws ensure compactness. Let w_{bv} be the number of atoms of type b in the molecule of type v . Then for all reactions r (except input and output) and all atom types b one has

$$\sum_{v \in I(r)} d_-(v, r) w_{bv} = \sum_{v \in O(r)} d_+(v, r) w_{bv}$$

Note that the limiting terms for input and output are

$$\sum_v (a_{v, in} - a_{v, out} c_v)$$

If there are no conservation laws then in general the trajectory can go to infinity or can reach a fixed point for finite time. The proof of the theorem for this case see in [17].

2.2 Unitarity and invariance of the Poisson measure

The condition for the invariance of the Poisson measure for the Markov process \mathcal{M}

$$\mu(n) = \prod_v \frac{\bar{b}_v^{n_v}}{n_v!} e^{-\bar{b}_v}, \bar{b}_v = M b_v$$

where b_v are some fixed parameters, can be written as the equality of output

$$F_{out} = \mu(n) \sum_r \lambda_r(n) \quad (4)$$

and input

$$F_{in} = \sum_r \mu(n') \lambda_r(n'), n' = n + d_-(r) - d_+(r) \quad (5)$$

probability flows for any given state $n = (n_1, \dots, n_V)$. Note that by (2) the summation in the right-hand side of (4) is only over admissible reactions that

is on the reaction such that $n_v - d_-(v, r) \geq 0$, and in the right-hand side of (5) is over r such that $n'_v - d_-(v, r) = n_v - d_+(v, r) \geq 0$.

Using

$$\frac{\mu(n')}{\mu(n)} = \prod_v \bar{b}_v^{n'_v - n_v} \frac{n_v!}{n'_v!},$$

where $F_{in} = F_{out}$, we get, dividing by $\mu(n)$ and using the uniqueness of defining n'_v in terms of n_v and r : $n'_v - d_-(v, r) = n_v - d_+(v, r)$

$$\begin{aligned} & \sum_r M^{-m_-(r)+1} a_r \prod_v \bar{b}_v^{n'_v - n_v} \frac{n_v!}{n'_v!} n'_v \dots (n'_v - d_-(v, r) + 1) = \\ & = \sum_r M^{-m_-(r)+1} a_r \prod_{v \in I(r)} n_v \dots (n_v - d_-(v, r) + 1) \end{aligned}$$

or

$$\begin{aligned} & \sum_r M^{-m_-(r)+1} a_r \prod_{v \in I(r)} \bar{b}_v^{d_-(v, r) - d_+(v, r)} n_v \dots (n_v - d_+(v, r) + 1) \\ & = \sum_r M^{-m_-(r)+1} a_r \prod_{v \in I(r)} n_v \dots (n_v - d_-(v, r) + 1) \end{aligned}$$

Finally

$$\begin{aligned} & \sum_r M^{-m_+(r)+1} a_r \prod_{v \in I(r)} b_v^{d_-(v, r) - d_+(v, r)} n_v \dots (n_v - d_+(v, r) + 1) \\ & = \sum_r M^{-m_-(r)+1} a_r \prod_{v \in I(r)} n_v \dots (n_v - d_-(v, r) + 1) \end{aligned} \quad (6)$$

where $m_+(r) = m_-(r) - \sum_{v \in I(r)} (d_-(v, r) - d_+(v, r))$.

Theorem 2 *The following statements are equivalent:*

- 1) *The Poisson measure μ is invariant under the given system of chemical reactions;*
- 2) *(Stueckelberg condition, or unitarity condition) for any vector d one has*

$$\sum_{r: d_-(r)=d} a_r \prod_{v \in I(r)} b_v^{d_-(v, r)} = \sum_{r: d_+(r)=d} a_r \prod_{v \in I(r)} b_v^{d_-(v, r)} \quad (7)$$

Proof. By reversibility of the previous calculation we have proved that condition 1) is equivalent to the condition (6). Let us use the fact that for the polynomial of n_v equal zero it is necessary and sufficient that all coefficients of its quasimonoms were zero. Two equal monoms are defined by the vector

$$d = d_-(r) = d_+(r)$$

Note also that the scaling coefficients cancel, as $m_-(r) = m_+(r)$.

Note that condition (7) has sense also for classical deterministic chemical kinetics where it can be interpreted as follows: the sum of reaction rates creating

the (and only this) group of particles characterized by the vector d , is equal to the sum of reaction rates which annihilate this (and only this) group.

A. N. Rybko remarked that, under the condition of the existence of invariant Poisson measure, time reversal in a process of stochastic chemical kinetics brings to the process of the same type, but in general with other set of chemical reactions.

2.3 Reversibility in probability theory

Probability theory has its own notion of time reversibility. Stationary random process X_t is called time reversible, if the finite-dimensional distributions of the processes X_t and $Y_t = X_{-t}$ coincide. For Markov processes (for example, with denumerable number of states and continuous time) this definition is equivalent to the following detailed balance condition

$$\pi_i \lambda_{ij} = \pi_j \lambda_{ji} \quad (8)$$

where λ_{ij} are the transition rates, π is the invariant measure of the Markov process. The latter definition can be applied also to the time homogeneous but not stationary, that is to null recurrent and non-recurrent Markov processes, but only if there exists (now infinite) non-negative measure π on the state space, satisfying condition (8). This will be called reversibility with respect to measure π . If π equals one in each point, then reversibility is equivalent to the symmetry of the matrix (λ_{ij}) . That is why any reversible chain can be obtained from the chain with symmetric transition matrix by the transformation

$$\lambda_{ij} \rightarrow w_i \lambda_{ij} w_j^{-1}, w_i = \sqrt{\pi_i}$$

Kolmogorov criterion of reversibility of the Markov process with respect to measure π consists in the fulfillment of the inequalities

$$\lambda_{i_1 i_2} \lambda_{i_2 i_3} \dots \lambda_{i_n i_1} = \lambda_{i_1 i_n} \lambda_{i_n i_{n-1}} \dots \lambda_{i_2 i_1}$$

for any sequence of states i_1, \dots, i_n . Under this condition, using definition (8), measure π is easily constructed as

$$\pi_{i_n} = \pi_0 a_{0i_1} a_{i_1 i_2} \dots a_{i_{n-1} i_n}, a_{ij} = \frac{\lambda_{ij}}{\lambda_{ji}}$$

for any sequence of states i_1, \dots, i_n , where

$$\pi_0^{-1} = 1 + \sum_k a_{G(0,k)}$$

where the sum is over all states $k \neq 0$, $G(0, k)$ is some path from 0 to k , that is a sequence of states i_0, i_1, \dots, i_n such that $i_0 = 0, i_n = k$, and

$$a_{G(0,k)} = a_{0i_1} a_{i_1 i_2} \dots a_{i_{n-1} i_n}$$

2.4 Chemical reversibility

The notion of chemical reversibility can be introduced in the general framework of Markov chains. Assume that on a given state space X be given some finite set \mathbf{A} of transition matrices $\lambda_{mn}^\alpha, m, n \in X, \alpha \in \mathbf{A}$ for some continuous time Markov chains. The elements of the set \mathbf{A} will be called “chemical reactions”. Assume that on \mathbf{A} the involution operation is defined - the reverse reaction $\alpha \rightarrow \alpha' \neq \alpha$, so that $(\alpha')' = \alpha$.

Define the Markov chain $\xi_{\mathbf{A}}$ on X by the transition rates

$$\lambda_{mn} = \sum_{\alpha} \lambda_{mn}^{\alpha}$$

We call such chain chemically reversible, if there exists a probability distribution π_n on X , that is for all α the following condition is holds

$$\pi_n \lambda_{nm}^{\alpha} = \pi_m \lambda_{mn}^{\alpha'}$$

In classical chemical kinetics the inverse reaction r' to the reaction r is uniquely defined by the conditions $d_-(r) = d_+(r'), d_-(r') = d_+(r)$.

For classical kinetics the detailed balance condition - that is the equality of the rates of direct and inverse reactions - looks as follows

$$a_r \prod_{v \in I(r)} b_v^{d_-(v,r)} = a_{r'} \prod_{v \in I(r')} b_v^{d_-(v,r')} \quad (9)$$

We shall see the difference between conditions (8) and (9).

Theorem 3 *Let the chemical reaction system be given where for any reaction r there exists an inverse reaction \bar{r} , Then the following conditions are equivalent:*

- 1) *The corresponding Markov process is chemically reversible;*
- 2) *The chemical reaction system is reversible (as the random process) with respect to some Poisson measure.*

Proof.

(1 \rightarrow 2) For a pair r, r' of two mutually inverse reactions the condition of chemical reversibility is

$$\pi_n a_r \prod_v \frac{n_v!}{(n_v - d_-(v,r))!} = \pi_{n'} a_{r'} \prod_v \frac{n'_v!}{(n'_v - d_+(v,r))!} \quad (10)$$

for some measure π_n and for any $n, n' = n - d_-(r) + d_+(r)$. Denote

$$z_n = \log(\pi_n \prod_v n_v!)$$

then instead of (10) we have

$$z_n - z_{n'} = \log \frac{a_{r'}}{a_r} \quad (11)$$

Denote l_r the right-hand side of (11), it is called the equilibrium constant in chemistry. Is we assume that in the given chemical reaction system \mathbf{A} all vectors

$$d = d(r) = d_-(r) - d_+(r), r \in \mathbf{A}$$

are different then we can consider l_r as a function $l(d)$ of $d = d(r)$. However it can occur that different reactions have equal vectors $d(r)$. Anyway, we have the following properties of $l(d)$:

1. from the right-hand side of (11) and from $d(r) = -d(r')$, it follows $l(d) = -l(-d)$;
2. from the left-hand side of (11) it follows: if for some sequence of reactions r_1, \dots, r_k one has $\sum_{i=1}^k d(r_i) = 0$, then

$$\sum_{i=1}^k l(d(r_i)) = 0$$

From these two properties it follows that $l(d)$ can be extended to an (additive) homeomorphism ϕ of additive subgroup $Q \subset Z^V$ to R , where V is the number of molecule types in the system, and Q is generated by all vectors $d(r)$, that is

$$\phi(0) = 0, \phi(x + y) = \phi(x) + \phi(y)$$

This homomorphism can be extended to the additive homomorphism of Z^V to R . Any such homomorphism can be written as

$$\phi(x) = \sum_v \alpha_v x_v$$

for some real numbers α_v .

Now one can check that the Poisson measure

$$p_n = \prod_v \frac{\alpha_v^{n_v}}{n_v!} e^{-\alpha_v} \quad (12)$$

satisfies condition (10). We have

$$w_n = \log(p_n \prod_v n_v!) = - \sum_v \alpha_v n_v + \text{const}$$

and hence, for any pair of vectors n, n' such that $n' = n - d_-(r) + d_+(r)$, we get

$$w_n - w_{n'} = \sum_v \alpha_v d_v(r) = l(d(r)), l(d(r)) = \log \frac{a_{r'}}{a_r}$$

It follows that the measure p_n satisfies equation (11) or, that is equivalent (10). Hence, the considered Markov chain has this measure as a stationary distribution, moreover it is reversible with respect to this measure.

(2 \rightarrow 1) Reversibility condition of the Markov process with respect to the Poisson measure (12) is that for any two vectors n, n'

$$p_n \sum_r a_r \prod_v \frac{n_v!}{(n_v - d_-(r))!} = p_{n'} \sum_{r'} a_{r'} \frac{n'_v!}{(n'_v - d_+(r))!} \quad (13)$$

where the summation is over all reactions r such that $n_v - n'_v = d_-(r) - d_+(r)$ and $n_v \geq d_-(r)$ for all v . From (13) it follows that

$$\prod_v \alpha_v^{n_v} \sum_r a_r \prod_v \frac{1}{(n_v - d_-(r))!} = \prod_v \alpha_v^{n'_v} \sum_{r'} a_{r'} \prod_v \frac{1}{(n'_v - d_+(r))!}$$

Hence

$$\sum_r a_r \prod_v \alpha_v^{d_-(r) - d_+(r)} \frac{1}{(n_v - d_-(r))!} = \sum_{r'} a_{r'} \prod_v \frac{1}{(n_v - d_-(r))!}$$

under the same agreement concerning summation. Otherwise speaking

$$\begin{aligned} \sum_r a_r \prod_v \alpha_v^{d_-(r) - d_+(r)} n_v \dots (n_v - d_-(r) + 1) &= \\ &= \sum_r a_r \prod_v n_v \dots (n_v - d_-(r) + 1) \end{aligned}$$

for fixed n_v and $d(r)$. As n_v are arbitrary, the latter equation can hold only if for the vector $d_-(r)$ (and corresponding vector $d_+(r) = d(r) + d_-(r)$) the following equality holds

$$a_r \prod_v \alpha_v^{d_-(r) - d_+(r)} = a_{r'}$$

This condition is obviously equivalent to the chemical reversibility for the Poisson measure (10) and to the detailed balance condition (9) as well.

Remark 4 *The Schloegl example, see below section 3.1, shows, that the stochastic reversibility does not imply the invariance of a Poisson measure.*

2.5 Large number of types

We do not give here exact formulations but indicate interesting classes of problems. The models where V is large, physically may correspond to two quite different situations, that we consider below. In the first case the system is subdivided into large number of cells. One can imagine that the cells form some space subdivision. In each cell the number of substance (molecule) types is bounded. Any substance can react only with the substances from the same cell or neighbor cells, the number of neighbor cells is also bounded. In the second case the number of substance types in each cell may be large. Moreover, even if the number of atom types is bounded, the number of atoms in a molecule can

be very large. Even more, most interesting situations appear when the reaction rates are large, that is the life time of these substances are short. Then all substances influence the evolution of the system. Substances with short life time correspond to the so called metastable molecules or clusters, as they are called in chemistry.

Locally finite reaction networks We will introduce them for the case when

$$\sum_v d_+(v, r), \sum_v d_-(v, r)$$

are uniformly bounded in r , and

$$\sum_r d_+(v, r), \sum_r d_-(v, r)$$

are uniformly bounded in v . Then V can be taken countable.

The infinite system of equations of classical kinetics can be deduced as above. Of course, M again has the sense of the volume but not the whole volume, but only local volume of each cell.

Unitarity condition and theorem 2 can be generalized to such infinite case. Markov reversibility condition is well-known for the locally interacting process, our system may fit to this case. In the same spirit the chemical reversibility condition can be generalized.

Models with large clusters Let we have only one type of elementary atoms and the clusters differ only by size. Formally speaking, we consider the partitions of the set with N elements-atoms into subsets which we call clusters. Let m_v be the number of clusters of size $v = 1, \dots, V$, that is consisting of v atoms, we assume the conservation law

$$\sum_v vm_v = N$$

but the number N initially can be random, the number of types V is fixed, but finally we will be interested with the asymptotics when $V \rightarrow \infty$. Define the Markov chain, the states of which are the vectors $m = (m_1, \dots, m_N)$. Possible reactions: 1) r_n - appending of a particle to a cluster of size $n > 1$

$$m_1 \rightarrow m_1 - 1, m_n \rightarrow m_n - 1, m_{n+1} \rightarrow m_{n+1} + 1,$$

and joining r_1 of the two particles

$$m_1 \rightarrow m_1 - 2, m_2 \rightarrow m_2 + 1$$

2) r'_n - separation of a particle from the cluster of size $n > 2$.

$$m_1 \rightarrow m_1 + 1, m_n \rightarrow m_n - 1, m_{n-1} \rightarrow m_{n-1} + 1$$

and decay r'_1 of two-particle cluster

$$m_1 \rightarrow m_1 + 2, m_2 \rightarrow m_2 - 1$$

Their rates $a_{r_n} = a_n, a_{r'_n} = a'_n$ do not depend of course on V, N . Assume that that chemical reversibility condition holds for any pair r_n, r'_{n+1} . Denote π the stationary Poisson distribution for this chain with parameters b_v . Then the chemical reversibility condition gives for all $n = 1, 2, \dots, V$

$$a_n b_1 b_n = a'_{n+1} b_{n+1}$$

These relations allow to construct many examples. In particular, for any given sequence of positive integers b_1, b_2, \dots one can uniquely find the fractions $\frac{a_n}{a'_n}$ of direct and inverse reaction rates. Some examples of this kind with concrete a_n, a'_n one can find in the book [11], where however small ensembles are considered.

3 Complexity of behavior and non-reversibility

3.1 Fixed points

Consider first the equations (3) of classical chemical kinetics. It appears that under the unitarity condition (hence, under reversibility conditions) their solutions have sufficiently simple behavior.

The Boltzmann entropy of the positive vector of concentrations $c = (c_1, \dots, c_V)$ with respect to some fixed non-negative measure c^0 on $\{1, \dots, V\}$ is defined as

$$H(c) = H(c, c^0) = \sum_v c_v \ln \frac{c_v}{c_v^0} + \sum_v c_v = \sum_v c_v \ln \frac{e c_v^0}{c_v}$$

Note that the factor e cannot be omitted, if the number of particles is not conserved. It is interesting that this expression is quite similar to the expression of entropy for mixture of ideal gases, see [9, 19].

Theorem 5 *Assume that for a given chemical reaction system there exists vector $c^0 > 0$, with respect to which the system satisfies the unitarity condition (7). The the following assertions hold:*

1) *for any solution $c_v(t)$ of kinetic equations (3) with any initial condition $c_v(0)$ the entropy is non-decreasing, that is*

$$\frac{dH(c(t))}{dt} \geq 0$$

2) *as $t \rightarrow \infty$ any solution $c(t)$ of equations (3) tends to some fixed point c_∞ , which in general depends on $c(0)$;*

3) *unitarity condition holds for any fixed point of equations (3);*

4) *if for some fixed point the detailed balance condition holds, it also holds for any other fixed point.*

Proof of these assertions can be found in [17].

Systems with one particle type Without unitarity condition such simple behavior is rarely possible. It is instructive to consider the following examples with one particle type. For one particle type and reactions $r : d_-(r) \rightarrow d_+(r)$ we have

$$\frac{dc(t)}{dt} = \sum_r (d_+(r) - d_-(r)) a_r c^{d_-(r)}(t) \quad (14)$$

where in the right-side part there can be arbitrary polynomial of c . We are interested only in non-negative solutions of this equation. Consider a particular case, the Schloegl model [28], where there are only reactions of types $0 \rightarrow 1, 1 \rightarrow 0, 2 \rightarrow 3, 3 \rightarrow 2$. Denote the corresponding a_r by $a_{01}, a_{10}, a_{23}, a_{32}$. It is not difficult to show that the unitarity condition holds only in the following three cases:

1. “input-output”: $a_{23} = a_{32} = 0$;
2. $a_{01} = a_{10} = 0$ - we call this case the closed Schloegl model;
3. if

$$\frac{a_{23}}{a_{32}} = \frac{a_{01}}{a_{10}}$$

One can show also that in these cases not only unitarity condition holds but also the detailed balance condition (9).

When in general first four coefficients of the polynomial 14 are different from zero, then on the positive half-axis there can be either one or three fixed points. In the latter case the right and left fixed points are stable, and the middle fixed point is unstable.

Remark 6 *For several molecule types the class of polynomials, corresponding to reactions with or without conservation laws, is sufficiently wide. As an example consider the set $R(I)$ of all reactions r , where $I = I(r) = O(r)$. Then*

$$\sum_{r \in R(I)} a_r (d_+(v, r) - d_-(v, r)) \prod_{v \in I} c_v^{d_-(v, r)}$$

that is we have an arbitrary polynomial.

It follows that non-reversible chemical reaction systems may have behavior of arbitrary complexity. For example, many systems with cycles are known [2]. It seems one can prove that chemical reaction systems can model any algorithmic behavior (that is any finite automata). From one side, it confirms unbounded possibilities of biological systems, and from other side it can be a source of artificial adjustment of the theory to experiment.

3.2 Fluctuations and Onsager relations

The behavior of systems in a neighborhood of a fixed point (that is close to the equilibrium) was much studied in statistical physics. Thus in the fluctuation theory for equilibrium dynamics (that is dynamics conserving the equilibrium

measure) one considers the neighborhoods of the concentrations c_v of the order $\frac{1}{\sqrt{M}}$, one can also perform linearization of the dynamical system in a small neighborhood - this is one of the ways to get Onsager relations. Now we give exact definitions.

Linearization and Onsager relations Consider small perturbations of the initial data $n_v(0)$, that is assume that the limits

$$c_v(0) = \lim_{M \rightarrow \infty} \frac{n_v^{(M)}(0)}{M}$$

belong to a small ϵ -neighborhood of the fixed point.

The linearization of the equations (3) around some distinguished solution $c_v(t)$ gives the following equations for the variations $x_v(t)$ of the solution $c_v(t)$

$$\frac{dx_v}{dt} = \sum_r a_r(d_+(v, r) - d_-(v, r)) \sum_u d_-(u, r) c_u^{d_-(u, r)-1} x_u \prod_{w \neq u} c_w^{d_-(w, r)}$$

In particular, if as a distinguished solution we take a fixed point $c_v(t) = \bar{c}_v$, then we have the system of linear differential equations with constant coefficients

$$\frac{dx_v}{dt} = \sum_r a_r(d_+(v, r) - d_-(v, r)) \sum_u d_-(u, r) \bar{c}_u^{d_-(u, r)-1} x_u \prod_{w \neq u} \bar{c}_w^{d_-(w, r)} \quad (15)$$

Rewrite it as

$$\frac{dx_v}{dt} = \sum_u \lambda_{vu} x_u \quad (16)$$

where the matrix of coefficients is

$$\lambda_{vu} = \sum_r a_r(d_+(v, r) - d_-(v, r)) d_-(u, r) \bar{c}_u^{d_-(u, r)-1} \prod_{w \neq u} \bar{c}_w^{d_-(w, r)} \quad (17)$$

Theorem 7 *Under the chemical reversibility condition the following Onsager relations hold*

$$\lambda_{vu} \bar{c}_u = \lambda_{uv} \bar{c}_v \quad (18)$$

Proof. From (17) we have

$$\lambda_{vu} \bar{c}_u = \sum_r a_r(d_+(v, r) - d_-(v, r)) d_-(u, r) \prod_w \bar{c}_w^{d_-(w, r)} \quad (19)$$

Assume now that the detailed balance condition holds both for direct and inverse reactions r, r'

$$a_r \prod_w \bar{c}_w^{d_-(w, r)} = a_{r'} \prod_w \bar{c}_w^{d_+(w, r)} \quad (20)$$

Then the contribution to the expression (19) from two mutually inverse reactions r, r' equals

$$\begin{aligned} & a_r(d_+(v, r) - d_-(v, r))d_-(u, r) \prod_w \bar{c}_w^{d_-(w, r)} + \\ & + a_{r'}(d_-(v, r) - d_+(v, r))d_+(u, r) \prod_w \bar{c}_w^{d_+(w, r)} \end{aligned} \quad (21)$$

The contribution from the same reactions to the expressions for $\lambda_{uv}\bar{c}_v$, similar to (19), equals

$$\begin{aligned} & a_r(d_+(u, r) - d_-(u, r))d_-(v, r) \prod_w \bar{c}_w^{d_-(w, r)} + \\ & + a_{r'}(d_-(u, r) - d_+(u, r))d_+(v, r) \prod_w \bar{c}_w^{d_+(w, r)} \end{aligned} \quad (22)$$

It is easy to see that the expressions (21) and (22) coincide. In fact, the terms containing the product's $d_-(u, r)d_-(v, r)$ and $d_+(u, r)d_+(v, r)$, in (21) and (22) are identical, and the remaining terms are equal correspondingly to

$$a_r d_+(v, r) d_-(u, r) \prod_w \bar{c}_w^{d_-(w, r)} + a_{r'} d_-(v, r) d_+(u, r) \prod_w \bar{c}_w^{d_+(w, r)}$$

and

$$a_r d_+(u, r) d_-(v, r) \prod_w \bar{c}_w^{d_-(w, r)} + a_{r'}(d_-(u, r) d_+(v, r) \prod_w \bar{c}_w^{d_+(w, r)})$$

But due to detailed balance condition (20) these expressions also coincide.

Entropy If the unitarity condition of Stueckelberg holds, then one explain the increase of the entropy $H(c)$ in a sufficiently simple and intuitive way. In fact, in this case the Poisson measure Q with the parameters $M\bar{c}_i$ is invariant. One can indicate a model where the dynamics leaves invariant the class of all Poisson measures, exactly (see section 4.1) or approximately. Thus, the Poisson measure P_t can change with time, and its parameters $M\bar{c}_i(t)$ depend on time somehow. Then the Kullback-Leibler divergence equals to

$$\rho_{KL}(Q, P_t) = \int P_t \ln \frac{P_t}{Q} = -M\tilde{H}(c)$$

where

$$\tilde{H}(c) = H(c) - \sum \bar{c}_i$$

(it is evident that $H(\bar{c}) = \sum_i \bar{c}_i$). On the other hand it is well known, that for any Markov process, under some technical conditions, $\rho_{KL}(Q, P_t)$ is monotone time decreasing, although possibly not strictly monotone. In this sense theorem 5 is a detalization of this general assertion.

The entropy $\tilde{H}(c)$ can be also interpreted in terms of probabilities of large deviations (where n is an arbitrary configuration)

$$\lim_{M \rightarrow \infty} \frac{\ln Q(n)}{M} = \tilde{H}(c)$$

if $\frac{n}{M} \rightarrow c$.

Fluctuations The fluctuations of the concentrations at time t , for fixed M , are defined as

$$\xi_v^{(M)}(t) = \xi_v^{(M, n_v(0))}(t) = \frac{n_v(t) - \langle n_v(t) \rangle}{\sqrt{M}} \quad (23)$$

This process depends, moreover, on the initial data $n_v(0)$, or from $\langle n_v(t) \rangle$. Equilibrium fluctuations correspond to the process $\xi_v(t+s)$ in the limit $s \rightarrow \infty$, when there is a stable fixed point $c_v^{fixed} = \bar{c}_v$ and

$$\lim_{M \rightarrow \infty} \frac{n_v(0)}{M} = c_v^{fixed} \quad (24)$$

Theorem 8 *Let the Markov process $\xi_v^{(M)}(t)$, for fixed M , be stationary and let the condition (24) hold. Then the limit (in the sense of finite-dimensional distributions) $(\xi_v(t))$ of the vector process $(\xi_v^{(M)}(t))$ as $M \rightarrow \infty$ is the Ornstein-Uhlenbeck process with mean 0 and covariance matrix*

$$D_{vv'}(t - t') = \langle \xi_v(t) \xi_{v'}(t') \rangle$$

defined by the formula (26) below.

Proof. For any fixed time, the vector $(\xi_v^{(M)}(t))$ has Poisson distribution, thus it converges in probability to a Gaussian vector $(\xi_v(t))$ which has moreover independent components and

$$\langle \xi_v(t) \rangle = 0, \langle \xi_v^2(t) \rangle = \bar{c}_i$$

Otherwise speaking the probability density of the vector $(\xi_v(t))$ is

$$\rho = \text{const} \exp\left(-\frac{1}{2} \sum_i \frac{x_i^2}{\bar{c}_i}\right)$$

The quadratic form in the exponent coincides with the quadratic part of the Taylor expansion of the function $H(\bar{c})$ at the point $c = \bar{c}$. That is, the covariance matrix β^{-1} is diagonal with diagonal elements \bar{c}_i . By definition, the matrix of kinetic coefficients $\gamma = \lambda \beta^{-1}$. Thus it is

$$\gamma_{ij} = \lambda_{ij} \bar{c}_j$$

By theorem 7 this matrix is symmetric as expected.

Now we will describe the time correlations. If the limit of the process $\xi_v^{(M)}(t)$ exists, then it is a stationary and reversible process, as it is stationary and reversible for all M . From central limit theorem it follows even more, see ([14, 15]). Namely, in the limit $M \rightarrow \infty$ this process is Gaussian with the generator

$$L = \sum_{v,w} D_{vw} \frac{\partial^2}{\partial x_v \partial x_w} + \sum_v b_v \frac{\partial}{\partial x_v}$$

where

$$b_v(x) = \sum_u \lambda_{vu} x_u$$

that is the drift is defined by linearized kinetic equations (16), see also [23].

This can be checked by a straightforward calculation: the drift at point (n_1, \dots, n_V) is equal to

$$\begin{aligned} S_v(n_1, \dots, n_V) = \\ = \sum_r (d_+(v, r) - d_-(v, r)) a_r M^{-m(r)+1} \prod_w n_w (n_w - 1) \dots (n_w - d_-(w, r) + 1) \end{aligned} \quad (25)$$

Put

$$c_v^{(M)} = \frac{n_v}{M}, s_v = \frac{S_v}{M}$$

Consider the stable fixed point $\bar{c}_v^{(M)} = \frac{\bar{n}_v}{M}$, where in particular

$$s_v = O\left(\frac{1}{M}\right)$$

In the $M^{-\frac{1}{2}}$ -neighborhood of this point, more exactly for the points $q_v M^{-\frac{1}{2}}$, let us find the vector field of drifts, already up to $M^{-\frac{1}{2}}$. For this substitute

$$c_v = \bar{c}_v + x_v M^{-\frac{1}{2}}$$

into (25). The resulting expression is similar to the expression for linearized system (15). The conservation laws holds here as well. Hence, in the limit we get a Markov process with linear drift, that is Ornstein-Uhlenbeck process, as the unique reversible stationary Gaussian process.

The diffusion matrix can be found from the condition of stationarity of the Gaussian measure

$$L^* \rho = 0$$

This condition leads to the equation

$$D\beta = -\lambda$$

or

$$D = -\lambda \beta^{-1} = -\gamma$$

Otherwise speaking, the diffusion matrix coincides with the matrix of kinetic coefficients. This connection between D and β holds of course in the general theory of equilibrium fluctuation as well [9]. The multi-time covariance

$$\phi_{vw}(t) = \langle \xi_v(t) \xi_w(0) \rangle, t > 0$$

can be found from the system of linear equations

$$\frac{d\phi}{dt} = \lambda\phi$$

with initial condition $\phi(0) = \beta^{-1}$. Thus

$$\phi(t) = e^{\lambda t} \beta^{-1} \quad (26)$$

The symmetry of the matrix ϕ is obvious. In fact, Onsager relations can be written as $\lambda' = \beta \lambda \beta^{-1}$, where the prime means transposition. Thus

$$e^{\lambda' t} = \beta e^{\lambda t} \beta^{-1}$$

which means that the matrix $e^{\lambda t} \beta^{-1}$ is symmetric.

Kubo formula Consider the matrix of kinetic coefficients $\gamma_{uv} = \lambda_{uv} \bar{c}_v$. In a neighborhood of the fixed point let us compare the quadratic covariance form and the quadratic part of the Boltzmann entropy. Both depend on the chemical reaction system and are defined by the reduction procedure of the quadratic forms with the conservation laws.

For the speed process

$$J_v(t) = \frac{d}{dt} \xi_v(t)$$

its covariance matrix

$$\vartheta_{vw}(t) = \langle J_v(t) J_w(0) \rangle$$

is

$$\vartheta(t) = -\frac{d^2}{dt^2} \phi(t) = -\lambda^2 \phi(t), t > 0$$

From this the famous Kubo formula (more exactly its classical variant) follows

$$\int_0^\infty \vartheta(t) dt = \gamma$$

where γ is the matrix of kinetic coefficients.

3.3 How non-reversible reaction systems come into play

The problem of time non-reversibility is the central problem in physics, and even more in biology. Thus it would be important to understand what elementary sources of non-reversibility could be in general.

Non-reversibility is related to the openness of the system, in particular with transitions like transport. For example, introduction of inputs, outputs or transport channels between reactions, also introduction of complementary substances. This can be realized physically by external fields (gravity, electromagnetic fields), current, in which the reactions occur, or with difference of diffusion constants.

Other source of non-reversibility are various analogs of the famous Boltzmann idea, called the Boltzmann-Grad limit in mathematical physics. There are many other parameters in closed systems the scaling of which allows to get non-reversible systems. For example, large deviations in the system can be considered as a special scaling in the initial state, when the system is driven far away from equilibrium and then one can follow the path of reaching the equilibrium.

3.3.1 Transport

Let we have several closed system of chemical reactions. One could join them together, allowing transport of substance from one system i to another j . We will say then that there is a transport channel from i to j . We want to show that after appending transport to the system it becomes in general non-reversible.

Consider a closed chemical reaction system, satisfying the detailed balance condition (9) with parameters b_v of the Poisson measure. Introduce in addition inputs and outputs, as mutually inverse reactions, for some substances with parameters $a_{in,v}, a_{out,v}$. For the system to stay chemically reversible these parameters should satisfy the following restriction

$$b_v = \frac{a_{in,v}}{a_{out,v}}$$

Consider now two independent closed systems and connect it by the transport channel with rates

$$a_{12,v}n_{1,v}, a_{21,v}n_{2,v}$$

where $n_{i,v}$ is the number of molecules of type v in the system $i = 1, 2$. Again we get that the condition (9) will hold only for one value of the parameters $\frac{a_{12,v}}{a_{21,v}}$.

3.3.2 Constant concentrations

In chemical kinetics one often encounters the assumption that one or more substances have constant concentrations. The first question is when the chemical reaction system with constant concentrations of some substances is non-reversible.

Consider a reversible system R of chemical reactions with substance from the set V . Let b_v be the concentrations, satisfying the detailed balance condition. Fix somehow the concentrations c_v from the set $W \subset V$, in general they different from b_v . Consider the reduced system of reactions with the substances from the set $V \setminus W$, assuming that there is no reactions where enter only substances from W .

Then the numbers $\phi(v) = \frac{c_v}{b_v}$ should satisfy the equation

$$\prod_v \phi(v)^{d_-(v,r)} = \prod_v \phi(v)^{d_+(v,r)}$$

for any reaction $r \in R$. Thus, the function $h(v) = \ln \phi(v)$ is an additive first integral for any reaction $r \in R$, that is

$$\sum_v d_-(v,r)h(v) = \sum_v d_+(v,r)h(v)$$

Here $h(v), v \in W$, are some given positive numbers, the rest $h(v), v \notin W$, are variables. Denote \mathcal{L} the set of all additive integrals of our system of chemical reactions, and \mathcal{H}_W is the subspace, consisting of the functions $f(v)$ such that $f(v) = \ln \frac{c_v}{b_v}$ for $v \in W$. The dimension of this subspace equals $|V| - |W|$. Thus, if $|W| > \dim \mathcal{L}$, then generically (that is for some open everywhere dense set of values $c_v, v \in W$) the intersection $\mathcal{L} \cap \mathcal{H}_W$ is empty. The exceptional values of the parameters $c_v, v \in W$, are the projection of the subspace \mathcal{L} on the coordinate plane $\{c_v, v \in W\}$ and cannot fill in all this plane if $|W| < \dim \mathcal{L}$. Thus, if in the reversible system R we fix $k+1$, where $k = \dim \mathcal{L}$, then the resulting system in general will not be reversible.

Example 9 For a system of reactions with atoms C, O, H of carbon, oxygen and hydrogen one has three first integrals - conservation of the numbers of these atoms. For sufficiently reach systems of reactions in organic chemistry there are no other independent integrals. Thus here $k+1 = 4$.

Remark 10 If there are reactions with substances only from W , then they can be excluded from the list of reactions of the reduced system. If the exclusion of these reactions does not change $\dim \mathcal{L}$ (for example, if the reaction r can be changed to a chain of reaction), then the previous conclusion persists, as they are based only on the comparison of $\dim \mathcal{L}$ and $|W|$.

Above it was essential that, up to the exclusion of these reactions, the detailed balance condition of the reduced system coincides with the detailed balance condition for the initial system. For the unitarity condition and the fixed points this is already not true.

Formally, one can get constant concentration, for example of one substance v_0 , using various scaling limits. One of the possibilities is to take the concentration v_0 big enough, moreover in the rates (2) of the Markov process one substitutes Mn_{v_0} instead of n_{v_0} , or, that is the same, to subtract $d_-(v_0, r)$ from $m_-(r)$. Then the limiting kinetic equations

$$\frac{dc_v(t)}{dt} = f(c_1, \dots, c_V)$$

will be

$$\frac{dc_v(t)}{dt} = f(c_v, v \neq v_0, c_{v_0})$$

$$\frac{dc_{v_0}(t)}{dt} = 0, c_{v_0}(0) = c_{v_0}$$

Alternative way is to introduce input and output v_0 , which have large rates $a_{v,in}, a_{v,out}$, so that the stationary distribution of the process “input-output” has a fixed value. Evidently, we will get constant concentration in the limit.

Inverse problem How to get given non-reversible reaction from reversible ones ? Consider some non-reversible system R_n consisting of several pairs of mutually inverse reactions. They are defined by the rates a_r . Note that for some values a_r this reaction system is reversible. Assume that in each reaction r some substances (enzymes) $w = w(r)$ participate. That is why in the expression (2) for the reaction rates there should be factor c_w . If one assumes as above that $c_{w(r)}$ are constant, then the rates a_r change to $a_r c_{w(r)}$, and by adjusting the concentrations $c_{w(r)}$ one can get necessary values a_r .

4 Stochastic local models

4.1 Stochastic models with mixed dynamics

Classical chemical kinetics is the typical example of what is called mean field theory in physics. Also, mixed models are possible where the reactions are described by mean field models, but some local transport is introduced as well. These models are useful for joining together chemical kinetics and chemical thermodynamics in ONE microscopic model. In the models introduced in [19], the mean field dynamics for chemical reactions is complemented by the free movement of particles. These models allow to deduce main laws of chemical thermodynamics. Here we describe only the limiting dynamics itself, referring the reader for all applications to [19, 20].

Dynamics of finite system of particles Firstly, define the dynamics of finite particle system in the volume $\Lambda \subset R^3$ with periodic boundary conditions. At time $t = 0$ we throw N particles to this volume, uniformly and independently, where N is random and has Poisson distribution with the density $\frac{\langle N \rangle}{\Lambda} = c$. To each particle we prescribe independently the type j and velocity v , which has density $p_0(j, v)$ (with respect to Lebesgue measure)

$$\sum_j \int p_0(j, v) dv = 1$$

Assume for simplicity that only binary reactions exist

$$r = (j, v), (j_1, v_1) \rightarrow (j', v'), (j'_1, v'_1) \quad (27)$$

If the velocities took only finite number of values then the chemical reaction system could be defined exactly as in section 1. In case of continuous velocities

instead of parameters a_r in (2) we introduce the rate densities, that is integrable (in all four variables) functions

$$a_r(((j_1, v_1), (j'_1, v'_1)|(j, v), (j', v')) \geq 0$$

Thus, each particle i changes its type and velocity at random moments

$$t_{i1} < t_{i2} < \dots$$

In the intervals between these moments the particle moves with constant velocity, obtained in the latter reaction.

Dynamics of the infinite system Consider the set \mathbf{X} of countable locally finite configurations $X = \{x_i, v_i, j_i\}$ of particles in R^3 , where each particle i has coordinate x_i , velocity v_i and type j_i . Denote \mathfrak{M} the set of all probability measures on \mathbf{X} with the following properties:

- the coordinates of these particles are distributed as the homogeneous Poisson point field on R^3 with some fixed density c ;
- the vectors (j_i, v_i) are distributed with common density $p(j, v)$,

$$\sum_j \int_{R^3} p(j, v) dv = 1,$$

independently of the coordinates and other particles.

Random dynamics on \mathbf{X} is given by the pair $(\mathbf{X}^{0,\infty}, \mu)$, where $\mu = \mu^{0,\infty}$ is the probability measure on the set $\mathbf{X}^{0,\infty}$ of countable arrays $X^{0,\infty}(t) = \{x_i(t), v_i(t), j_i(t)\}$ of piecewise linear trajectories $x_i(t), v_i(t), j_i(t), 0 \leq t < \infty$. It is assumed that the measure μ belongs to the family $\mathfrak{M}^{0,\infty}$ of measures on $\mathbf{X}^{0,\infty}(t)$, defined by the following properties:

- if for any t we denote $\mu(t)$ the measure induced by the measure μ on \mathbf{X} , then $\mu(t) \in \mathfrak{M}$. Denote

$$c_t(j, v) = c_t p_t(j, v)$$

where c_t, p_t are the concentration- and the densities at time t ;

- the trajectories $(x_i(t), v_i(t), j_i(t))$ are independent for different i and each of them is a trajectory of some Markov process, not necessarily time homogeneous. This process is defined by the initial measure $\mu(0) \in \mathfrak{M}$ and by infinitesimal transition probabilities at time t , moreover the latter do not depend on coordinates, velocities and types of other particles, but depend on $c_t(j, v)$ at time t ;

- the evolution of the pair (j, v) for individual particle is defined by the following Kolmogorov equation

$$\begin{aligned} \frac{\partial p_t(j_1, v_1)}{\partial t} = \\ = \sum_j \int (P(t; j_1, v_1 | j, v) p_t(j, v) - P(t; j, v | j_1, v_1) p_t(j_1, v_1)) dv \end{aligned}$$

where

$$P(t; j_1, v_1 | j, v) = \sum_{j', v'_1} \int 2a_r((j_1, v_1), (j'_1, v'_1) | (j, v), (j', v')) c_t(j', v') dv' dv'_1$$

Note that in the reactions there can be energy conservation law, see [18, 19], then the integration in the last formula includes the corresponding δ -functions;

- coordinates of the particle i change as

$$x_i(t) = x_i(0) + \int_0^t v_i(s) ds$$

Let the measure $\mu(0) \in \mathfrak{M}$ be given. Consider now the sequence of finite system of particles, defined above, in an expanding system of finite volumes $\Lambda \uparrow R^3$. The initial measure for any of finite systems is the restriction of the measure $\mu(0)$ on the corresponding volume Λ . Hence, at the initial moment we can fix a separate particle i in R^3 and can consider its trajectories $x_i^{(\Lambda)}(t)$ in each Λ , starting from some. Besides this, its trajectory $x_i(t) \in \mathbf{X}^{0, \infty}$ is defined in R^3 .

We have seen that two definitions - for finite and infinite particle systems - are quite different. The following result shows how they are related.

Theorem 11 *For any i and t we have the convergence in probability*

$$\lim_{\Lambda \uparrow R^3} x_i^{(\Lambda)}(t) = x_i(t)$$

Proof see in the Appendix to the paper [19].

4.2 Boltzmann equation with chemical reactions

4.2.1 Model and result

Assume that at time $t = 0$ in the cube $\Lambda \subset R^d$ there are $N < \infty$ particles, each particle is characterized by the coordinate $x \in \Lambda$, velocity $v \in R^d$ and type $q \in \{1, \dots, Q\}$. The initial vector $(x_i(0), q_i(0), v_i(0) : i = 1, \dots, N)$ will be denoted by ω_0^Λ . Assume that the initial measure μ_Λ on the set ω_0^Λ of configurations in Λ

is defined by the probabilities p_N that the number of particles in Λ equals N , and by the conditional densities (for given N)

$$\rho_{N,\Lambda}(x_1, v_1, q_1, \dots, x_N, v_N, q_N) < C^N$$

symmetric with respect to the permutation group S_N . and normalized so that

$$\frac{1}{N!} \sum_{q_1, \dots, q_N} \int \rho_{N,\Lambda} \prod_{k=1}^N dx_k dv_k = 1$$

Then the k -particle correlation functions are defined as

$$f_k(x_1, v_1, q_1, \dots, x_k, v_k, q_k) = \sum_{N=k}^{\infty} \frac{p_N}{(N-k)!} \sum_{q_{k+1}, \dots, q_N} \int \rho_{N,\Lambda} \prod_{j=k+1}^N dx_j dv_j$$

Hence, the probability that in any of small volumes $dx_i dv_i, i = 1, \dots, k$ there is a particle of type q_i , is equal to

$$f_k(x_1, v_1, q_1, \dots, x_k, v_k, q_k) \prod_{i=1}^k dx_i dv_i \quad (28)$$

For any initial configuration ω_0^Λ define the continuous time Markov process

$$\xi(t, \omega) = \xi_{N,\Lambda}(t, \omega, \omega_0^\Lambda) = (x_i(t), v_i(t), q_i(t) : i = 1, 2, \dots, N)$$

In the defined system the randomness related to the initial (for $t = 0$) configuration is denoted by ω_0^Λ , and the randomness related to the random jumps is denoted by ω . Heuristically $\xi(t, \omega)$ is defined as the mixture of deterministic (piecewise linear) dynamics (with periodic boundary conditions) for the coordinates and random jumps for the velocities and types. These random jumps are assumed to be binary reactions, which change velocities and types. More exactly, the velocities and types are assumed to be piecewise constant on $[0, \infty)$; the jumps occur at random time moments

$$0 < t_1(\omega) < \dots < t_k(\omega) < \dots \quad (29)$$

On the time intervals $t \in (t_i, t_{i+1}]$ the particle move freely $\frac{d^2 x_i(t)}{dt^2} = 0$, that is with constant velocities $v_k(t) = v_k(t_i + 0)$. Thus almost everywhere we have $v_k(t) = \frac{dx_k(t)}{dt}$. Thus, the coordinates at time $t \in R_+$ are defined as

$$x_i(t, \omega) = x_i(0) + \int_0^t v_i(t, \omega) dt$$

At the same time any pair of particles i, j (independently of the other pairs) on any time interval $(t, t + dt)$ change their types and velocities with the rate (rate densities)

$$\lambda(q'_i, v'_i, q'_j, v'_j | x_i(t), v_i(t), q_i(t), x_j(t), v_j(t), q_j(t)) dt$$

The functions λ are assumed non-negative, bounded, smooth, translation invariant and equal zero, if at least one of the following conditions holds:

1. $|x_i - x_j| \geq 2r$;
2. for some $v^0 > 0$ either $|v'_i| > v^0$ or $|v'_j| > v^0$.

These jumps do not change coordinates, but change velocities and types

$$(q_i, v_i, q_j, v_j) = (q_i, v_i, q_j, v_j)(t) \rightarrow (q'_i, v'_i, q'_j, v'_j) = (q'_i, v'_i, q'_j, v'_j)(t + 0)$$

Denote

$$\begin{aligned} B(v, q, v', q' | v_1, q_1, v_2, q_2) &= \\ &= \lambda(v, q, v', q' | x, v_1, q_1, x, v_2, q_2) \end{aligned}$$

Thus, for given N, Λ, λ, r we have defined the family $\xi_{N, \Lambda}(t)$ of processes with finite number of particles.

Remark 12 *This model allows many generalizations, for example when the movement of particles between jumps is defined by the Hamiltonian system with pair potential $V(x - y)$ and interaction radius r*

$$\frac{d^2 x_i(t)}{dt^2} = - \sum_{j: j \neq i} \frac{\partial V(x_i - x_j)}{\partial x_i}$$

Initial conditions We consider the family μ_r of initial distributions in a finite volume Λ or in R^3 with correlation functions $f_k^{(r)}(0; x_1, v_1, q_1, \dots, x_k, v_k, q_k)$, parametrized by positive numbers r (interaction radii). It is assumed that this family satisfies the following conditions:

1. (Boltzmann-Grad scaling) For some fixed bounded non-negative function $f(x, v, q)$

$$f_1^{(r)}(0; x, v, q) = r^{-d+1} f(x, v, q) \quad (30)$$

This scaling says that the mean density of particles grows as r^{-d+1} as $r \rightarrow 0$. Note that simultaneously “effective” volume Nr^d (r can be considered as “effective” radius of the particles), occupied by the particles, tends to zero as r ;

2. (exponential decay of correlations)

$$\begin{aligned} &|f_2^{(r)}(0; x_1, v_1, q_1, x_2, v_2, q_2) - f_1^{(r)}(0; x_1, v_1, q_1) f_1^{(r)}(0; x_2, v_2, q_2)| < \\ &< C \exp(-C_1 r^{-1} |x_1 - x_2|) \end{aligned}$$

for all positive sufficiently small $r \rightarrow 0$:

3. (strong stability) The number of particles $n(A)$ in arbitrary volume $A \subset \Lambda$ is uniformly bounded a.s. by $c r^{-d+1} |A|$ for some $c > 0$. It is a physically natural condition;

4. (bounds from above) for some $C > 0$

$$f_k^{(r)}(0; x_1, v_1, q_1, \dots, x_k, v_k, q_k) < C^k r^{(-d+1)k}, k \geq 1$$

Let us give an example of a point field, satisfying conditions 1-4. Consider first the Poisson field with the correlation functions

$$g_k(x_1, v_1, q_1, \dots, x_k, v_k, q_k) = \prod_{i=1}^k g_1(x_i, v_i, q_i)$$

for some smooth bounded functions g_1 . Define μ_r as the point field, obtained from the Poisson field with k -particle functions $g_k^{(r)} = r^{(1-d)k} g_k$ by the transformation F on the set of configurations, where the configuration $\omega_1 = F(\omega_0)$ is obtained from ω_0 by deleting any particle for which in ω_0 there is another particle on the distance less or equal to $2r$. Then the properties 1,3 follow from the definition. The property 4 follows from the monotonicity

$$f_k^{(r)} \leq g_k^{(r)}$$

The property 2 follows from standard estimates of the probability that there exists a cluster (a sequence of particles with the distance not more than $2r$ of subsequent particle from the previous) of the diameter $\frac{1}{2}|x_1 - x_2|$, containing at least one of the particles x_1 or x_2 .

4.2.2 Existence of cluster dynamics

We say that two particles i, j interact at time t , if at this moment a reaction occurred between them, in particular at this moment the distance between them was not more than $2r$. Denote s_{ij} the first moment of interaction of particles i and j . Consider the following finite random graphs $G^\Lambda = G^\Lambda(\tau) = G^\Lambda(\tau, \omega)$. Their vertexes are the particles, it is convenient to enumerate them with their initial vectors $x_i(0)$. Two vertexes are connected by the edge if on the time interval $[0, \tau]$ these vertexes interacted at least once. For fixed τ and Λ the set of vertexes of any connected component of the graph $G^\Lambda = G^\Lambda(\tau)$ is called a dynamical cluster (in Λ).

If at point x at initial moment there is a particle then denote $P_k^\Lambda(\tau|x)$ the conditional probability that the dynamical cluster to which this particle belongs, consists of exactly k particles. Put

$$\rho = \max_x \sum_q \int f_1(x, v, q) dv$$

Then the following exponential estimate holds, see [21].

Theorem 13 *Their exist constants $C, \alpha_0 > 0$ such that for any τ, v^0, r and*

$$\rho = \alpha(\tau v^0 r^{d-1})^{-1} \quad (31)$$

with arbitrary $0 < \alpha < \alpha_0$ uniformly in k, Λ, x the following inequality holds

$$P_k^\Lambda(\tau|x) \leq (C\alpha)^{k-1}$$

Remind that the expression for the density has the following meaning: the mean number of particles $\langle N \rangle$ in the unit volume, multiplies on maximal volume of the tube, covered by the particle (that is $2r$ -neighborhood of its trajectory), were less than some α_0 . Proof see in [21].

From this theorem it follows that with probability 1 any particle on the time interval $[0, \tau]$ belongs to a finite cluster depending on the chosen particle and on the initial configuration. Moreover, there is the thermodynamic limit which is the cluster dynamics in R^d . Otherwise speaking, the dynamics of infinite number of particles is obtained from infinite number of independent finite particle dynamics.

More exactly, there is the following cluster representation of the dynamics. Consider the Markov process $\xi_k(t) = (x_1(t), v_1(t), q_1(t), \dots, x_k(t), v_k(t), q_k(t))$ on the time interval $[0, \tau]$ with k particles (assuming the absence of other particles), if initially the particles were at points $\xi_k = \xi_k(0) = (x_1, v_1, q_1, \dots, x_k, v_k, q_k)$. Let us denote $\gamma = \gamma(\eta|\xi)$ the trajectory of the process $\xi_k(t)$ starting at time 0 at point ξ and ending at time τ at the point $\eta = (x'_1, v'_1, q'_1, \dots, x'_k, v'_k, q'_k)$. Denote $P^\tau(\gamma(\eta|\xi))$ the conditional distribution on the set $\{\gamma(\eta|\xi)\}$ of such trajectories. Let $\Gamma_k = \Gamma_k(\eta|\xi)$ be the set of all such trajectories γ , which form a k -cluster.

Then using (28) we get

$$\begin{aligned} f(\tau; x, v, q) &= \\ &= \sum_{k=1}^{\infty} \sum_{q_1, \dots, q_k}^{\infty} \int_{R^{dk} \times \Lambda^k} \prod_{i=1}^k dx_i dv_i \prod_{i=2}^k dx'_i dv'_i \int_{\Gamma_k} Q(\gamma) \\ &\quad dP^\tau(\gamma((x, v, q, x'_2, v'_2, q'_2, \dots, x'_k, v'_k, q'_k)|\xi)) f_k(0; x_1, v_1, q_1, \dots, x_k, v_k, q_k) \end{aligned}$$

where $Q(\gamma) = Q(\gamma(\eta|\xi))$ is the conditional probability that other particle in the configuration ω_0^Λ do not interact with the distinguished k particles.

4.2.3 Proof of the Boltzmann equation

If the existence of cluster dynamics holds for fixed r , then the Boltzmann equation holds only in the Boltzmann-Grad limit. Fix τ and v^0 and assume that the function $f(x, v, q)$ from the condition (30) is sufficiently small so that the conditions (31) holds.

Theorem 14 *Then in the Boltzmann-Grad limit for any $t < \tau$ there exist the density functions*

$$\lim_{r \rightarrow 0} r^{d-1} f^{(r)}(t; x, v, q) = f(t; x, v, q)$$

which satisfy the Boltzmann equation

$$\frac{\partial f}{\partial t}(x, v, q) = -v \frac{\partial f}{\partial x}(x, v, q) +$$

$$+ \sum_{q', q_1, q_2} \int [B(v, q, v', q' | v_1, q_1, v_2, q_2) f(x, v_1, q_1) f(x, v_2, q_2) - B(v_1, q_1, v_2, q_2 | v, q, v', q') f(x, v, q) f(x, v', q')] dv_1 dv_2 dv'$$

In the zeroth approximation (that is if there is no interaction) there are only 1-clusters and then

$$f(t + \delta; x, v, q) = f(t; x - v\delta, v, q) \quad (32)$$

Subtracting $f(t; x, v, q)$ from both sides of this inequality, dividing by δ and passing to the limit $\delta \rightarrow 0$, we get

$$\frac{\partial f}{\partial t} = -v \frac{\partial f}{\partial x}$$

In the general case the equality (32) corresponds to the event, that the particle which were at the point x, v at time t , did not react in the time interval $(t, t + dt)$.

In our case we can write

$$f(t + \delta; x, v, q) = f(t; x - v\delta, v, q) - A_1^{(r)} + B_1^{(r)} + O(\delta^2) \quad (33)$$

The term A_1 is obtained from the events, when at time t there were a particle with parameters $x - v\delta, v, q$, which in the sequel (in some time $s, t < s < t + \delta$) reacted with another particle, which at time t had the parameters x_1, v_1, q_1 . In other words

$$A_1^{(r)} = \sum_{q_1, q', q'_1} \int_t^{t+\delta} ds \int \lambda(q', v', q'_1, v'_1 | x(s), v(s), q(s), x_1(s), v_1(s), q_1(s)) f_2^{(r)}(t; x - v\delta, v, q; x_1, v_1, q_1) dx_1 dv_1 dv'_1 dv'_1$$

Note that as it follows from the cluster property, the decay of correlations is conserved for any time moment in the interval $0 < t \leq \tau$. Then

$$A_1^{(r)} \rightarrow \delta \sum_{q_1, q', q'_1} \int B(q', v', q'_1, v'_1 | v, q, v_1, q_1) f_1(q, v) f_1(q_1, v_1) dv' dv'_1 dv_1$$

The term $B_1^{(r)}$ appears from the events, when at time t there are two particles with parameters $x_1, v_1, q_1, x_2, v_2, q_2$, which react at time $s, t < s < t + \delta$ so that one of emerging particles has parameters x, v, q . Thus,

$$B_1^{(r)} = \sum_{q_1, q_2, q'} \int_t^{t+\delta} ds \int \lambda(v, q, q', v' | x_1, v_1, q_1, x_2, v_2, q_2) f_2^{(r)}(x_1, v_1, q_1, x_2, v_2, q_2) dx_1 dv_1 dx_2 dv_2 dv'$$

Similarly we have

$$\lim_{r \rightarrow 0} B_1^{(r)} = \delta \sum_{q_1, q_2, q'} \int B(v, q, q', v' | v_1, q_1, v_2, q_2) f_1(q_1, v_1) f_1(q_2, v_2) dv_1 dv_2 dv'$$

From the cluster representation of the dynamics it easily follows that the remaining clusters do not contribute to the Boltzmann equation, as they are of order $O(\delta^2)$.

Remark 15 *Other models and other techniques of proving the Boltzmann equation see in [33, 22, 34, 30, 31, 32, 29, 35].*

4.3 Simplest models with transport on the lattice

Let at each point x of the lattice Z^d there can be $n_v(x)$ particles of type $v = 1, 2, \dots, V$. In each point the Markov process $\xi_x = (n_1(x), \dots, n_V(x))$ is given, that is a chemical reaction system as defined in section 2. These processes are independent and have the same distribution. We add some terms to the generator of this process, which correspond to independent simple continuous time random walk for each of the particles, homogeneous in time and space. The parameters $\lambda_{e,v}$, that is the jump rates, where e runs $2d$ unit vectors along the axes, can depend only of the type v . Assume now that the drift vectors

$$m_v = \sum_e e \lambda_{e,v} \neq 0$$

for all v . We will use the scaling

$$x = \frac{X}{\epsilon}, t = \frac{\tau}{\epsilon}, \lambda_r(n) \rightarrow \epsilon \lambda_r(n)$$

where $X \in R^d, \tau \in R$ are macro-variables. In the definition (2) we put $M = 1$, so the number of particles in any point has the order $O(1)$. This scaling says in particular, that for finite macro-time τ at a given point there can be $O(\tau)$ reactions.

Theorem 16 *Let at the initial moment $t = 0$ the initial Poisson distribution*

$$\prod_x \prod_v \frac{(b_{v,x})^{n_v(x)}}{n_v(x)!} \exp(-b_{v,x})$$

of the particles on the lattice so that $b_{v,x} = c_v(0, \epsilon x)$ for some smooth bounded functions $c_v(0, X), X \in R^d$. Then as $\epsilon \rightarrow 0$ for any functions $x(\epsilon) : R_+ \rightarrow Z^d$ such that $\epsilon x(\epsilon) \rightarrow X$, there exist the limits of the concentrations

$$c_v(\tau, X) = \lim_{\epsilon \rightarrow 0} \langle n_v(\frac{\tau}{\epsilon}, x(\epsilon)) \rangle$$

which satisfy the equations

$$\frac{\partial c_v}{\partial \tau} = -m_v \frac{\partial c_v}{\partial X} + F_v(c_1, \dots, c_V) \quad (34)$$

where the functions F_v are the same as in the right-hand side of the equations (3).

Shortly, the ideas of the proof are as follows. Firstly, it is well-known and easy to prove, that under no reaction condition the independent particle satisfies the equation (34) without the last term. The reactions go much slower than the transport and for finite macro-time their number at each point is $O(1)$. Thus, at the intervals between reactions the distributions of different particle types at each point tend to become independent and have Poisson distribution with some parameters $c_{v,x}$, due to the fast mixing by random walks. Thus in the limit $\epsilon \rightarrow 0$ for any integer $k > 0$

$$< n_{v,x}(n_{v,x} - 1) \dots (n_{v,x} - k + 1) >_{Poisson} = c_{v,x}^k$$

The estimates for the convergence of limit transitions are based on one or another variant of cluster expansions. See more details of the proofs in [22], pp. 308-313, 315-316 and in the references therein.

If all drifts $m_v = 0$, then one needs another (diffusion) scaling

$$x = \frac{y}{\epsilon}, t = \frac{\tau}{\epsilon^2}, \lambda_r(n) \rightarrow \epsilon^2 \lambda_r(n)$$

which corresponds to the difference of the scales of reaction times and temperature movement. Here we get reaction-diffusion equations, if we assume the jump rates in each direction $\lambda_v = \frac{1}{2}$,

$$\frac{\partial c_v}{\partial \tau} = \frac{1}{2} \Delta c_v + F_v(c_1, \dots, c_V)$$

The ideas of the proof are similar to the previous theorem.

There is an interesting case when the coordinates of the drift are nonzero in one direction (current) and zero for perpendicular directions (diffusion). Let us consider, for example, the two-dimensional lattice $Z^2 = \{(x, y)\}$ with several particle types, where $m_{v,x} = 0, m_{v,y} \neq 0$ for all v . Then in the scaling

$$x = \frac{X}{\epsilon}, y = \frac{Y}{\epsilon^2}, t = \frac{\tau}{\epsilon^2}, \lambda_r(n) \rightarrow \epsilon^2 \lambda_r(n)$$

the limiting equations are

$$\frac{\partial c_v}{\partial \tau} = -m_{v,x} \frac{\partial c_v}{\partial Y} + \frac{1}{2} \frac{\partial^2 c_v}{\partial X^2} + F_v(c_1, \dots, c_V)$$

All kinetic equations, described above, may have several invariant measures if the corresponding equations

$$F_v(c_1, \dots, c_V) = 0$$

have several fixed points.

5 Chemical reaction as a process

5.1 Time reversibility in physics

A map (function, operator) f from the set A onto the set B is called invertible, if it is one-to-one, that is if there exists mapping $g = f^{-1}$ of the set B onto the set A such that gf is identical on A , then fg is identical B . Then f and g are called mutually inverse. If $A = B$, then f is called automorphism.

Automorphism U generates the automorphism group U^t , where $t \in Z$, and it is often possible to embed it into some continuous automorphism group with $t \in R$. The automorphism group of the set A is called time invertible with respect to the automorphism W of the set A , if

$$W^{-1}U^tWU^t = 1 \quad (35)$$

or $U^{-t} = W^{-1}U^tW$.

In physics the notion of time invertibility (reversibility) is related to concrete automorphisms (normally involutions) W . So; in the classical Newtonian physics of n particles one considers the automorphism groups of the manifold

$$\Lambda^n \times R^{nd} = \{(\bar{x}, \bar{p}) = (x_1, \dots, x_n, p_1, \dots, p_n)\}, x_i \in \Lambda \subset R^d, p_i \in R^d,$$

and W is taken equal

$$W(\bar{x}, \bar{p}) = (\bar{x}, -\bar{p})$$

In non-relativistic quantum mechanics A is a complex Hilbert space, automorphism group is a unitary group $U^t = \exp(itH)$ with the generator H , and W is an anti-linear map. For example, in some representation

$$W\phi = \bar{\phi}$$

If $HW = WH$, then (35) holds.

In relativistic quantum theory invertibility may take place for one operators W , but not for the other, as for parity violation.

Such physical invertibility, under certain conditions, implies reversibility of corresponding stochastic systems. Example is the reversibility of the transfer matrix in the euclidean approach to quantum field theory, the invertibility of the scattering matrix and reversibility of Markov processes, obtained in a weak interaction limit.

The scattering matrix $S : \mathcal{F} \rightarrow \mathcal{F}$ is the unitary operator in the Fock space $\mathcal{F} = \mathcal{F}(\mathcal{H})$, where \mathcal{H} is the direct sum of all one-particle subspaces \mathcal{H}_q in $\mathcal{F}(\mathcal{H})$. One-particle subspace corresponds to the type q particle. Let $e_{q,k}$ be some orthonormal basis in \mathcal{H}_q , where k corresponds to momentum. Let $\gamma = \{(q_1, k_1), \dots, (q_n, k_n)\}$ and consider the basis

$$e_\gamma = e_{q_1 k_1} \otimes \dots \otimes e_{q_n k_n}, n = 0, 1, \dots,$$

in \mathcal{F} . Denote the squares of the matrix elements of S in this basis by

$$|S(\gamma \rightarrow \gamma')|^2 = w(\gamma \rightarrow \gamma')$$

Then from the norm invariance it follows that

$$\sum_{\gamma'} w(\gamma \rightarrow \gamma') = \sum_{\gamma'} w(\gamma' \rightarrow \gamma) = 1 \quad (36)$$

that is the matrix $W = (w(\gamma \rightarrow \gamma'))$ is doubly stochastic.

Note that the condition (36) corresponds to the unitarity condition introduced in section 2. Intuitively, to get stochastic dynamics from unitary scattering matrix one could do as follows: introduce random waiting times in the states γ , then matrix W will play role of the matrix of conditional probabilities (at the end of waiting time) of jumps from γ to γ' . There is one more difficulty - γ depend on index k , which correspond to momenta, or to velocities. It is desirable that the process, obtained by restriction to the set of types $\{q\}$ would be Markov. And moreover, that the matrix W^0 , which is obtained by restricting the matrix W to the set of types, also be doubly stochastic. This would mean that there is restoration of classical chemical kinetics, which is normally defined without taking into account velocities. In [20] it is shown that under some conditions this really happens.

Under certain limiting transitions unitary quantum dynamics becomes stochastic, for example in the weak interaction limit, see for example [27], moreover one has reversible Markov process.

5.2 Classical Hamiltonian scattering

The first question is whether any bound state can be obtained dynamically by colliding its components. It is not always possible. It is simpler to see from the classical scattering theory, already for the simplest example of scattering of one particle on the center, see [1]. The main restriction is of course the energy conservation law, that is of the sum of internal and kinetic energies. We do not know whether it is the unique restriction.

Scattering of one particle on external potential Let us consider one-dimensional problem of scattering of one classical particle on smooth external potential $V(x)$, $x \in R$, equal zero outside some bounded interval. Let the particle move from $-\infty$ with speed v_0 . It is known that the formation of the bound state, that is the capture of the particle by the potential, is possible only for the set velocities of measure zero. This follows from the time invertibility of the dynamics. In fact, three cases are possible:

- 1) the particle changes the direction of movement. This can be only in the point where $\frac{dV}{dx} \neq 0$. Then the particle passes the same path in the opposite direction;
- 2) the particle stops. This can occur only in the points $\frac{dV}{dx} = 0$. The number of such values of v_0 is finite.
- 3) the particle passes to $+\infty$. Then it does not stop and does not change direction.

There similar results, see [1], for the one particle scattering on external potential for dimensions $d \geq 2$.

If however one may introduce the possibility of fast or momentary energy dissipation, for example when the energy is transferred to the third particle or to some internal degrees of freedom of the two particle cluster, then the formation of the bound state becomes possible. The particle can fall into the potential energy well.

Two-particle and three-particle scattering Two-particle scattering can be reduced to the previous case, and for three particles there are examples from celestial mechanics, see [16], which show what possibilities are possible.

5.3 Reaction rates from local theory

The following simple model shows how one can obtain reaction rates from local models.

Consider a free system of $N_i, i = 1, 2$, balls of radii r_i in the volume M , which move not seeing each other with Maxwell velocity distribution, that is in equilibrium. Denote $c_i = \frac{N_i}{M}$ the fractions of such particles. It is easy to prove that the number of binary reactions “collisions” of balls of different types on a large time interval $[0, t]$ is asymptotically equal to (if $N_i, M \rightarrow \infty$,)

$$R(N, M, t) \sim t N_1 N_2 \frac{4\pi(r_1 + r_2)^3}{3M}$$

Thus, the mean number of collisions for unit time and volume is equal to

$$\frac{R}{tM} = \frac{4\pi(r_1 + r_2)^3}{3} c_1 c_2$$

The part of energetic collisions, that is such that the sum of kinetic energies is not less than some number T_{cr} , is approximately

$$a_r \exp(-\beta T_{cr}) c_1 c_2$$

for some constant a_r , corresponding to a given reaction. This is the contents of the Arrhenius law.

Various mathematical problems, related to the transfer of chemical energy to kinetic energy see in [18, 19, 20].

5.4 Dynamics with non-momentary reactions

Let us consider the infinite system of point particles in R^d , where each particle is defined by the coordinate x , velocity v and type $j = 1, \dots, J$. The particles interact via pair potentials $U_{jj'}(x - x')$. It is assumed that the interaction radii are $R_{jj'}$, finite. Define the graph with vertexes in the particle coordinates, connecting two particles of types j, j' with an edge, if the distance between them does not exceed some $R_{jj'}$. To the vertex also we prescribe velocity and type of the corresponding particle. Consider connected finite marked graphs G with vertexes marked in this way. There are continuum of such graphs, and we

introduce the equivalence classes of such graphs. Two graphs G_1 and G_2 are called equivalent, if at least one of the following three conditions holds:

1. G_1 and G_2 are isomorphic as marked graphs, that is they are isomorphic as graphs and the marks of the corresponding vertexes coincide;
2. G_1 and G_2 are obtained from one another by shifting all coordinates with the same vector;
3. G_1 and G_2 are obtained from one another by Hamiltonian dynamics of the corresponding particle system with potentials $U_{jj'}(x - x')$ for finite time.

The equivalence class will be called cluster or metastable particle. Metastable particle is called stable, or a bound state, if it exists for infinite time under the absence of other particle.

Infinite system of particles in R^d at any time moment can be partitioned on (maximal) connected components. Each component corresponds to a cluster.

Assume now that there exists Gibbs equilibrium state for the given particle system (in particular, that the potential is stable). Then under some conditions, for example for small density of particles, one can prove that at any time moment all clusters are finite with probability 1. Moreover, some extended clusters (called above the dynamical clusters) stay finite on some on some time interval, see [21].

However, other problems, for example about the existence times of clusters are open. For example, it seems that (stable) bound states are absent with probability 1, except of course one-particle clusters. In fact, let we have for example only two types of particles 1, 2 and the potential V_{12} is such that the unique possible bound state consists of two particles, where one of the particles rotates around another with the circle orbit. Some relation between velocity of the rotation and the distance (radius of the circle orbit) between particles. But, as the distributions of coordinates and velocities are independent, this is possible only with zero probability.

From other side, there exist infinite number of metastable clusters, where these relations hold approximately, and clusters live sufficiently long and disappears either by itself or after collision with other cluster. Interesting problem is to estimate the life time of a cluster as depending of the parameters of the Gibbs distribution.

However, there are many other open questions concerning connection of the notion of particle in finite and infinite systems.

In finite particle systems, classical and quantum, one first introduces elementary particles. In the classical case as the point particles, in quantum case as creation-annihilation operators. The Hamiltonian can have also bound states. In classical case these are the orbits of some type, in quantum - eigenfunctions of the discrete spectrum. In some cases one can show that they completely determine possible asymptotic states of the system. In principle, bound states of any number of particles are possible.

If we consider infinite system, then there exists a certain theory only for equilibrium dynamics, that is the dynamics while the system is in the equilibrium (Gibbs) state. Here also elementary particles, called bare or unrenormalized particles, which however do not belong, contrary to the finite systems, to the discrete spectrum after the thermodynamic limit. New discrete spectrum can appear (more exactly, one particle states). The main hypothesis, proved in some cases, is that the pair (Hilbert space, Hamiltonian), corresponding to given infinite interacting system of particles, is unitary equivalent to some similar pair for a system of non-interacting particles, which are called then quasi-particles. These quasi-particles can be close to bare particles for example if the interaction is small. In physics a quasi-particle is often imagined as a particle surrounded by a cloud of other bare particles. This could give a bridge between quasi-particles in infinite systems and metastable states of finite systems, however there are no exact formulations and proofs.

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